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ART UNIT	PAPER NUMBER
1812	8

DATE MAILED: 01/21/92

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

Disclosure Statement

Response To Restriction Requirement

☒ This application has been examined ☒ Responsive to communication filed on 5/9/91 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s); 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

- | | |
|---|---|
| 1. <input checked="" type="checkbox"/> Notice of References Cited by Examiner, PTO-892. | 2. <input type="checkbox"/> Notice re Patent Drawing, PTO-948. |
| 3. <input checked="" type="checkbox"/> Notice of Art Cited by Applicant, PTO-1449. | 4. <input type="checkbox"/> Notice of Informal Patent Application, Form PTO-152 |
| 5. <input type="checkbox"/> Information on How to Effect Drawing Changes, PTO-1474. | 6. <input type="checkbox"/> |

Part II SUMMARY OF ACTION

1. ☒ Claims 1-10 are pending in the application.
Of the above, claims 6-9 are withdrawn from consideration.
2. ☐ Claims have been cancelled.
3. ☐ Claims are allowed.
4. ☒ Claims 1-5, 10 are rejected.
5. ☐ Claims are objected to.
6. ☐ Claims are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed has been ☐ approved; ☐ disapproved (see explanation).
12. ☒ Acknowledgement is made of the claim for priority under U.S.C. 119. The certified copy has ☒ been received ☐ not been received ☐ been filed in parent application, serial no. ; filed on
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

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Serial No. 07/369,686
Art Unit 1812

-2-

Receipt is acknowledged of papers submitted under 35 U.S.C. § 119, which papers have been placed of record in the file.

5 Applicant's election with traverse of Group I, claims 1-5 and 10 in Paper No. 7 is acknowledged. The traversal is on the ground(s) that it would not constitute undue burden to search the invention of Group II, claims 6-9, with those of Group I. This is not found persuasive because burden has previously been established as shown by the different classification and the
10 necessity for non-coextensive literature searches for Groups I and II.

15 The requirement is still deemed proper and is therefore made FINAL.

Claims 6-9 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 7.

20 35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of
25 this title".

Claim 5 is rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter.

Claim 5 is drawn to a use of a compound which is a non-statutory invention.

30 Claims 2-4 are rejected under 35 U.S.C. § 101 because the invention as disclosed is inoperative and therefore lacks utility.

35 Claims 2-4 appear to be drawn to pharmaceutical compounds containing the precursor protein of claim 1. However, no pharmaceutical utility has been demonstrated for this protein. Its disclosed utility is as an intermediate that is cleaved to form a variant of insulin. There is no evidence of record that

this precursor has any biological activity.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-5 are rejected under 35 U.S.C. § 102(b) as being anticipated by Markussen et al. (EPO 163,529).

Claims 1-5 are rejected under 35 U.S.C. § 102(e) as being anticipated by Markussen et al. (U.S. Patent No. 4,946,828).

Both Markussen et al. references disclose the insulin variant B(1-29)-Arg-A(1-21) of human insulin produced recombinantly in yeast. As such, this precursor protein before cleavage and the method of producing the cleaved human insulin variant are inherently disclosed. (See column 15; Table 1, column 17, and claims in '828.) This information has been incorporated into the patent from EPO 163,529. (See column 14, lines 42-43.) Both references further teach use of the insulin variants as pharmaceuticals.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the

time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5 Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same
10 person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various
15 claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order
20 for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claim 10 is rejected under 35 U.S.C. § 103 as being unpatentable over Markussen et al. (EPO 163,529) or Markussen et al. (U.S. Patent No. 4,946,828) either in view of Goeddel et al.
25 (EPO 055,945).

Both Markussen et al. references are applied as above.

Goeddel et al. teaches producing recombinant fusion proteins of insulin fused to another protein. The reference further teaches making a fusion protein with an insulin variant in which
30 the C chain of insulin contains only six amino acids. (See page 6, line 19 through page 8, line 2; abstract; claims; page 26-27.)

It would have been obvious to make the fusion proteins of Goeddel et al. using the insulin variant taught by either Markussen et al. reference. One would have been motivated by the

known benefits of producing small peptides as fusion proteins in microorganism hosts and the success with another insulin variant in which the C chain is shortened.

5 The following is a quotation of the first paragraph of 35 U.S.C. § 112:

10 The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15 The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description and enabling disclosure.

20 Claim 5 recites a "one-pot reaction". The specification does not clearly describe what is intended by such a reaction. It is unclear whether this limitation of claim 5 is enabled by the specification.

 The structure of formula II in claim 5 is not described nor its formation enabled by the specification. (See specification page 2.)

25 Claim 10 is drawn to a fusion protein with a ballast component. However, "ballast component" is not defined in the specification and it is unclear whether this limitation of claim 10 is enabled by the specification.

 The specification contains numerous occurrences of numerals

in parentheses throughout the description of various DNA and vector constructions (e.g. page 11, lines 18-22). It is not clear what these numbers refer to. In some cases they appear to correspond to oligonucleotide sequences present in Tables 1 and 2 and in other cases they appear to correspond to the Figures. Some could correspond to either. The specification is ambiguous and confusing. Applicants are cautioned against introducing new matter in clarifying the specification.

Claims 1-5 and 10 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 2-5 and 10 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite for failing to clearly indicate that the compound of formula I is a single peptide chain with all amino acids contiguous. It is ambiguous to define "B(1-30)" and "A(1-21)" as the B and A chain of human insulin because these chains are known to be cleaved and attached to each other by disulfide bonds. As such, it is unclear what structure applicant is claiming, particularly how and where the additional arginine ("Arg") amino acid is connected to the structure.

Claims 2, 3, and 10 are duplicative of claim 1. Claim 2 is

drawn to compound of the formula I, claim 3 is drawn to a pharmaceutical containing the compound of formula I, and claim 10 is drawn to a fusion protein containing the compound of formula I. However, neither of these claims adds further limitations to the compound of formula I in claim 1. The phrase "for use as a pharmaceutical, in particular for the treatment of diabetes mellitus" in claim 2 is functional language and given no patentable weight. While claim 3 is drawn to a pharmaceutical, no additional components are required to distinguish this compound from that of claim 1. While claim 10 is drawn to a fusion protein, no additional protein component is required to be fused to formula I. The phrase "preferably bonded...of the fusion protein" is functional language and given no patentable weight.

Claim 4 would be clearer if it recited a "pharmaceutical composition" or something of this nature rather than "pharmaceutical" alone.

Claim 5 is indefinite in reciting "the -S-S- bridges are arranged as in insulin, or of insulin, preferably in a one-pot reaction". It is unclear what the term "arranged" encompasses. It is unclear what the phrase "or of insulin" is intended to mean. It is not known what a "one-pot reaction" encompasses. The specification does not provide a clear description for this type of reaction and what it encompasses.

Claim 5 appears to contain typographical errors that render

it indefinite. The structure of formula II in this claim is drawn incorrectly. Please see specification at page 2. There are two extra bonds connecting the sulfur atoms on lines 3 and 4 of this structure.

5 Claim 10 is indefinite in reciting "ballast component". The specification does not provide a clear description for this phrase and what it encompasses. Claim 10 is also indefinite in reciting "preferably bonded via a bridging member". This is not a clear limitation of the claim and furthermore provides no
10 indication of how or where (N-terminal or C-terminal) the bridging member is located or whether the bridging member, ballast component and compound of formula I are operably linked.

 Claims 2-5 and 10 are indefinite in reciting "of the formula I". Claims 2-4 and 10 are independent claims and as such, it is
15 not clear "what of formula I" is in reference to. It appears that these claims should be dependent upon claim 1. While claim 5 is nominally dependent upon claim 1 it is only dependent upon it with respect to the definitions of "A(1-21)" and "B(1-30)" and not to define the structure of formula I.

20 The Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1812.


25 Papers related to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1
30 Fax Center number is (703) 308-4227.

Serial No. 07/369,686
Art Unit 1812

-9-

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne Porta Allen whose telephone number is (703) 308-0666.

5 Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.


DAVID L. LACEY
SUPERVISOR PRIMARY EXAMINER
ART UNIT ~~180A~~

11/1/92